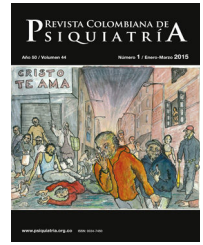




REVISTA COLOMBIANA DE PSIQUIATRÍA

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Reporte de caso

Case Report of Retarded Catatonia: Always Consider Catatonia as a Differential Diagnosis of Altered Mental Status

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ARTICLE INFO

Article history:

Received 24 September 2021

Accepted 2 February 2022

Keywords:

Catatonia

Benzodiazepines

Electroconvulsive therapy

ABSTRACT

Background: Catatonia is a rare neuropsychiatric condition; it is estimated that around 10% of patients with mood disorders present signs and symptoms of catatonia. A catatonic syndrome is characterised by mutism, negativism, rigidity, and stupor.

Case report: We report the case of a 59-year-old patient with a medical history of bipolar disorder who was admitted to the internal medicine service due to a seizure episode. During hospitalisation, the patient presented significant worsening of her clinical condition, showing marked symptoms of stupor and catatonia. Once the neurological and metabolic etiologies of altered mental status had been ruled out, pharmacological treatment with high doses of lorazepam was started. The patient had a complete clinical remission, and her evolution was favourable without any complications. Electroconvulsive therapy was recommended as a definitive treatment.

Conclusions: The diagnosis of catatonia is a challenge for both hospitalists and psychiatrists due to the clinical presentation of catatonia. In reporting this clinical case, we want to emphasise the importance of taking into account the catatonic syndrome in our differential diagnoses in patients with altered mental status.

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Informe de un caso de catatonia retardada: Considerar siempre la catatonia como diagnóstico diferencial de la alteración del estado mental

RESUMEN

Introducción: La catatonia es una condición neuropsiquiátrica poco frecuente, se estima que cerca del 10% de los pacientes con trastornos afectivos presentan signos y síntomas de catatonia. El síndrome se caracteriza clínicamente por mutismo, negativismo, rigidez y estupor.

Palabras clave:

Catatonia

Benzodiazepinas

Terapia electroconvulsiva

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Caso clínico: Se describe el caso clínico de una paciente de 59 años con antecedentes de trastorno bipolar, ingresada por el servicio de medicina interna por un episodio de crisis convulsiva. Durante la hospitalización, la paciente presentó un importante deterioro clínico, marcado estupor y síntomas de catatonía. Una vez descartadas etiologías neurológicas y metabólicas de la alteración del estado de conciencia, se inició el tratamiento farmacológico con altas dosis de lorazepam. El cuadro clínico de la paciente evolucionó favorablemente con una remisión clínica completa.

Conclusiones: El diagnóstico de catatonía constituye un reto tanto para médicos internistas como psiquiatras por su presentación clínica. Con el reporte de este caso clínico se desea enfatizar la importancia de considerar al síndrome catatónico en nuestros diagnósticos diferenciales en pacientes con alteración del estado de conciencia.

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Introduction

Catatonia is a medical condition associated with mood-affective disorders, schizophrenia, neurological and medical conditions; it is characterized by an inability to move, mutism, rigidity, and refusal to eat, among others. To date, there are two types: retarded and excited.^{1,2} Some prospective studies suggest that catatonia can be observed in 10% of patients at psychiatric units and in up to 30% of patients admitted to medical wards.³

Imbalances in the excitatory-to-inhibitory ratio (EIR) at the spinal and brainstem level may play a role in the etiology.⁴ In addition, research reported that the GABA pathway has a part in the suppression of the immune response.⁵ This is why some patients with catatonia respond to agonists of GABA-A receptors.

Catatonia can be diagnosed based on clinical suspicion, at least four catatonic symptoms must be present for a diagnosis. In addition, a trial of lorazepam is required to support the diagnosis.⁶ Catatonia can be challenging when doctors are trying to obtain a medical history and physical examination because patients manifest with mutism, and so this lack of information can difficult a correct diagnosis, assessment, and plan.^{2,7} Is not a rare medical condition encountered at the emergency department and in the acute care setting, but due to the diverse presentation of catatonia, it can be misdiagnosed.^{6,8}

Patients with catatonia and comorbid mood disorders can resolve their condition completely with benzodiazepine treatment and electroconvulsive therapy.⁹ Moreover, some cases will need a specialized level of care, nasogastric tube placement, intravenous fluids, and anticoagulation to decrease morbidity and mortality.¹⁰

Case presentation

The patient is a 59-year-old woman with a background of longstanding cirrhosis, bipolar disorder, and major depressive disorder with psychotic features, stable on alprazolam, fluoxetine, and lurasidone. It allowed her to live an independent life. The patient was brought to the behavioral facility complaining

about increased agitation, auditory and visual hallucinations (she was seeing bugs on her arms, hair, and on the wall as well as seeing a red light that was coming out from the television), uncooperative, no insight into her condition and judgment severely impaired. In the facility, the patient was started on a tapering dose of clorazepate (Tranxene 7.5 mg) detoxification schedule with thiamine and folic acid. As per the mother and medical staff, the patient developed an episode of tonic-clonic seizure, which prompted them to transfer her to the ER. Upon admission, her vital signs were temperature of 101.4, tachycardic to 116, and slightly hypertensive. On examination, the patient was posturing, staring stuporous, nonverbal, nonresponsive, flat affect, stiff, increased tone of four extremities, and waxy resistance to passive movement. She had, another episode of seizure in the ER, and an initial diagnosis of possible sepsis, benzodiazepine withdrawal, or hepatic encephalopathy was made. She was admitted to the Internal Medicine ward, and extensive neurologic, infectious, and toxicologic work-up (amphetamine, barbiturates, opioids negative, and benzodiazepines positive) was done including lumbar and imaging such as CT head without contrast, CT angiography of the neck, EEG, echocardiogram, and chest x-ray which were normal. Ammonia level was elevated just on admission. The patient failed swallow evaluation and was placed on NPO, metoprolol IV, and lorazepam 1 mg IV BID, and levetiracetam 500 mg BID. Throughout hospitalization, her mental status decline progressively despite the use of lactulose for metabolic encephalopathy and with only short episodes of lucidity shortly after being administered IV benzodiazepines, but she remained with mutism, not following commands, looking in space, mumbling. Despite her presentation, the impression was that she was suffering from acute retarded catatonic syndrome secondary to her bipolar affective disorder. Psychiatry and Internal Medicine agreed to start a trial of IV benzodiazepines at a therapeutic dose for catatonia (lorazepam 3 mg IV every 8 h). After the administration of lorazepam patient improve substantially and progressively, initially somewhat catatonic, but later able to verbalize again with better eye tracking and able to ask for water and her mood was euthymic. She was able to follow simple commands without difficulty, the patient presented a favorable evolution without any complications A final recommendation to the

Table 1 – Signs and symptoms of Acute Catatonia by Karl Kahlbaum et al².

Sign	% Of patients
Immobility	97
Mutism	97
Withdrawal and refusal to eat	91
Staring	87
Negativism	67
Posturing	58
Rigidity	54
Waxy flexibility/cataplexy	27
Stereotypy	25
Echolalia or echopraxia	14
Verbigeration	14

patient was to be transferred to a hospital that had electroconvulsive therapy for definitive treatment.

Discussion

Diagnosis of acute catatonia is a challenge for both hospitalists and psychiatrists because it is difficult to obtain a complete medical history from a mute patient. In this context, it is primordial to be sure that some medical conditions such as non-convulsive status epilepticus, stroke, abulia, akinetic mutism, delirium, and dementia are not present at diagnosis.² Moreover, neurological emergencies (neuroleptic malignant syndrome NMS), need to be ruled out before considering acute catatonia as those conditions need a prompt diagnosis, treatment, and admission to the medical intensive care unit (MICU).¹¹

According to Karl Kahlbaum, catatonia is diagnosed when a patient has at least 4 of 11 signs and symptoms.² The most common signs and symptoms of catatonia are immobility and mutism; those are present in about 90% of cases (Table 1).²

Treatment of catatonia should be started as soon as catatonia is suspected and is critical for a good patient's progress and recovery. In all cases of catatonia, the underlying disorder (e.g. undiagnosed bipolar disorder) has to be addressed. It is a priority to discontinue any potential hazardous drugs that cause catatonia such as dopamine antagonists, anticonvulsants, and antipsychotics, etc.⁶

Current recommendations are based on the general condition of the patient. For instance, non-life-threatening catatonia is treated by the administration of benzodiazepines. If the patient responds within one week, there is no need to continue the benzodiazepine medication at discharge. However, if the patient has a slow response (clinical response after the first week) there is a need to initiate electroconvulsive therapy.¹²

Among the most common benzodiazepines (GABA agonist drugs) used in catatonia are lorazepam and clonazepam.^{11,13} Initially, it is recommended to start with a dose of 2 mg of lorazepam intravenously. If there is a good response, it is advised to schedule the drug up to three times a day.⁶

Benzodiazepines' response has been demonstrated in many studies, a clinical response is achieved within 3 hours after the administration of lorazepam. The oral route is

preferred, however, when that is not feasible an intramuscular or intravenous route should be used. Most patients recovered their baseline clinical state with a lorazepam dose between 1 to 3 mg.^{14,15} As the patient's mental state improves focus should be placed on the underlying medical condition.⁶ In our case, no organic cause was identified and we focused on treating the acute catatonic state.

Duration of therapy varies according to clinical response; some patients might need a single dose and other patients might require multiple doses or even a continuous infusion. Response to therapy can be evaluated by the Bush-Francis catatonia scale.¹⁵ After a therapeutic dose of lorazepam is achieved, tapering of the drug should be done slowly to prevent a new episode of catatonia.⁶

Research about other therapeutic options than lorazepam is controversial and non-conclusive. Current treatments studied for catatonia are clonazepam, antipsychotics (olanzapine), dantrolene, amantadine, and zolpidem which have been reported good results.¹⁶⁻¹⁸

Antipsychotics have been evaluated in patients with catatonia and an underlying psychotic condition. Among the antipsychotics studied, there is clozapine, which is a low-affinity dopamine receptor agonist. Clozapine showed a beneficial effect in psychotic patients.¹⁵ The use of second-generation (atypical) antipsychotics was preferred over traditional first-generation because of the lower risk of developing neuroleptic malignant syndrome.¹³ Even though antipsychotics were used in some cases, the current recommendation is against the use of all dopamine blocking drugs (antiemetic agents, first and second-generation antipsychotics) because all antipsychotics might worsen catatonia. If the underlying disorder is a psychotic condition that needs antipsychotic medication, the antipsychotic drug could be resumed with extreme caution only once the patient is stable, eating and drinking adequately, and without any signs of catatonia.¹²

Clonazepam was used in some studies only after achieving an initial response with lorazepam. Clonazepam was preferred over lorazepam in patients who needed longer hospitalization. The pharmacologic properties of clonazepam, a longer half-life, were well suited for patients suffering from catatonia and COVID-19 pneumonia.¹⁹

Olanzapine and lorazepam, as a combination therapy, showed a good response in patients with catatonia secondary to anti-NMDA receptor encephalitis. Olanzapine alone was not as effective as in combination with lorazepam to improve agitation.²⁰

Zolpidem has been studied in cases of resistant catatonia in adolescents. The drug has a similar mechanism of action to lorazepam, a positive allosteric effect on GABA-A receptors. However, zolpidem binds to a specific subunit (alpha1) rather than a non-specific site on the receptor. Zolpidem might be a non-benzodiazepine alternative in cases of resistant catatonia, although more research is needed.²¹

According to Freitas de Lucena et al.¹⁵, 500 mg of amantadine intravenously can be beneficial in the treatment of catatonia as many motor scores showed a complete improvement after a couple of hours. However, amantadine is not routinely used because has dopamine agonist properties and can exacerbate psychotic symptoms.¹²

Electroconvulsive therapy (ECT) is a well-studied treatment for catatonia. ECT in combination with benzodiazepines is recommended as initial treatment in patients with life-threatening (malignant) catatonia. In addition, ECT is recommended in patients who did not respond within the first week of lorazepam administration.¹²

In some studies, the frequency of bilateral ECT was three-time per week. In addition, unilateral ECT was preferred over bilateral to prevent cognitive impairments such as headaches and memory loss. These adverse effects might be related to the frequency of electroconvulsive therapy.¹⁵ In our patient, lorazepam was the initial treatment and ECT was considered as a definitive treatment. Multiple studies showed a recovery rate of up to 80% with lorazepam alone, ECT alone, and ECT after lorazepam.¹²

There are common complications in catatonia such as refusing to eat, dehydration, pneumonia, pressure ulcers, deep venous thrombosis, and pulmonary embolus.^{2,6} In the last decade, catatonia has had an excellent response (80%) and prognosis to benzodiazepines (lorazepam). The patients who do not respond to lorazepam usually have a bad prognosis later.^{6,15}

Conclusions

Catatonia is underdiagnosed due to the lack of awareness of the condition among both medical doctors and psychiatrists. We always have to consider acute catatonia syndrome among our differential diagnoses for altered mental status.

As catatonia is a highly treatable condition, there must be a high suspicion to diagnose and treat this disease. Failure to do so increases the morbidity and mortality outcome among patients.

More research is required to do a catatonia protocol, thereby it is important to have further data on patients with catatonia.

ECT has proved to be efficacy in refractory catatonia, as well as in the incomplete response to benzodiazepines.

Conflicto de intereses

The authors declare no conflict of interest.

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